

maximum antiluetic therapy even in secluded places or while away from home.

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URINARY TRACT INFECTIONS

FROM A GENERAL PRACTICE STANDPOINT

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PART II*

DISCUSSION by Charles Pierre Mathé, M.D., San Francisco; Harry W. Martin, M.D., Los Angeles; Frank Himman, M.D., San Francisco.

BY far the commonest of urinary infections are those of the ascending type, one of the more frequent being associated with the passage of catheters into the bladder. The passage of a urethral catheter on a postoperative patient, followed in twelve or twenty-four hours by a chill and pyuria, is frequently interpreted as indicative of faulty technique in its sterilization, or undue trauma by the nurse or house officer officiating. It is now generally accepted by urologists, however, that the primary cause of such ascending infection has occurred prior to the catheterization. The trauma that has resulted from allowing the bladder to become overdistended being the true etiologic factor, whoever is responsible for the delay in ordering catheterization should accept the blame for the subsequent ascending infection—with its elevated temperature, chills, and fever—rather than the one who actually performed the catheterization. There seems little question that the custom of waiting for surgical patients to void after their bladders have filled is responsible for a far greater number of acute renal infections than the poor technique of nurse or house officer who did the catheterization. Nothing so sets the stage for immediate urinary infection as the overdistention of any part of the urinary tract. The stretching of the mucosa causes a serious hemorrhagic exudate which, in the presence of urine, seems to be the finest of culture media.

ASCENDING RENAL INFECTION

All urologists can attest to the distressing febrile reactions following the first drainage of an uninfected and frequently unsuspected hydronephrosis. Ascending renal infection stands, today, as the most common cause of death associated with the drainage of the overdistended bladder in prostatic obstruction. In this group should undoubtedly be included those disturbances following cystoscopic examination described by the comforting title, post-cystoscopic reactions or, in the jargon of the specialist, cystoreactions.

Such an attack of acute ascending infection is usually characterized by frequency, dysuria, fever and, if particularly severe, chills, and was treated, until the decade previously referred to, more or less successfully by the administration of methenamin. Its effect was known to depend upon the liberation of formaldehyd, which could only occur in an acid media, and so acid sodium phosphate was also prescribed to insure acidity of the urine. This method of treatment met with failure in all cases in which the urine remained alkaline, either because of the simultaneous ingestion of alkalizing drugs, or more frequently, due to the presence of a mixed infection in which were included urea-splitting organisms constantly liberating ammonia. In other cases the liberation of the formaldehyd resulted in so much irritation to the urinary mucosa that the symptoms were aggravated rather than improved. When such unfortunate results developed, it was customary to reverse the process by the administration of alkalizing drugs. If the urine was already alkaline, this, of course, brought no relief.

The effect of acid and alkaline values on the power of growth of organisms in the urine is not a new discovery. Kitasabo in 1888 showed media of different acid values will kill, inhibit or allow typhoid or cholera organisms to grow. In 1917 Quinby suggested the investigation of the effect of acids in inhibiting the growth of bacteria in the human being, and Shohl and Janeway later proved that *B. coli* are inhibited in urine at p^H of 4.6 to 5.0 on the acid side, and 9.2 to 9.6 on the alkaline side. The p^H values for the acid side can easily be obtained by the administration of drugs; but it is not possible in the human being to obtain alkaline values sufficiently high to inhibit the growth of organisms, and not until the degree of acidity or alkalinity in urine could be accurately and easily determinable by calorimeter methods, was rational therapy possible.

ACIDITY AND ALKALINITY: p^H SCALE

Acidity and alkalinity have long been recognized as important factors in practically all branches of research and industrial work. Although it has proved its value and been widely adopted in so many different lines of work, many still hesitate to use p^H methods because they feel that its application requires the services of trained experts. Such misapprehension should not exist, since it is almost as easy to make p^H determinations as it is to make measurements of the rise and fall of the temperature. All are familiar with the Fahrenheit thermometer. On its scale, 32 degrees represents

* For Part I, see CALIFORNIA AND WESTERN MEDICINE, April, 1939, on page 254.

the freezing point. For the sake of illustration, let us assume that values above or below 32 degrees represent degrees of heat and coldness, respectively. Thus, any value higher than 32 degrees denotes an increase in heat, the degree of heat increasing as the numbers increase. On the other hand, any value below 32 degrees denotes an increase in coldness, the decrease in coldness increasing as the numbers decrease.

In a similar manner the degree of acidity or alkalinity of a solution is expressed by the p^H scale. Instead of being called degrees, as in the case of the thermometer, the units on this scale are called p^H values. It is apparent that it is not necessary for a person to know the derivation of the term "degree Fahrenheit" in order to determine the temperature of a solution with a thermometer, nor is it essential that one should know the derivation of the term " p^H " in order to measure the acidity or alkalinity of a solution.

On the p^H scale the value of p^H 7.0 represents neutrality. The solution is neither acid nor alkaline. Values higher than 7 denote alkalinity, the degree of alkalinity increasing as the numbers increase. Any value lower than p^H 7 denotes acidity, the degree of acidity increasing as the numbers decrease. This increase or decrease is measured in multiples of 10. Thus, a solution with a p^H of 5 is ten times as acid as one with p^H of 6.0, or a p^H of 4.0 indicates an acidity a hundred times as great as a p^H of 6.0.

The principle of making p^H measurements is based on the fact that various indicators change color when they are acted upon by solutions of different acidities or alkalinities. Until recently it was impossible, except in careful laboratory experiments, to tell the degree of acidity or alkalinity one was dealing with, as the determination of the reaction of urine was ascertained usually by litmus. Now, however, the exact percentage of acidity or alkalinity can be determined by simply dropping a piece of Squibb's nitrazine paper in the urine and comparing it with a color chart. Such accuracy was not possible with litmus paper, for its color range runs from p^H 4.6 to 8.4, which amounts to 3.8 p^H units, and experiment has shown that p^H values of 6.6, 6.7, 7.4, and 7.9 will appear neutral to litmus, while values of 6.8, 6.9, and 7 are recorded as alkaline.

Other indicators, such as chlorphenol red and bromthymol blue, change within a range of 1.6 p^H units and so are more accurate. For the practitioner no indicator is as satisfactory as Squibb's nitrazine papers, which are accurate to one-half unit readings.

ALKALINITY

Although it was shown experimentally that bacterial growth could not be inhibited by any degree of alkalinity obtainable in the human urine, the belief in its clinical virtues persists, based on the following: That the acidity of the urine rather than the products of bacterial growth are responsible for the irritated mucosa with its associated burning, frequency, and tenesmus. In fact, the idea that increased acidity will produce untoward symptoms is so firmly fixed in the human mind that we find

the unscrupulous, by a campaign of fear, proclaiming this accepted fact in their national advertising in order to dispose of still greater and greater quantities of alkalinizing drugs. Indeed, today soda fountains are taking on the character of virtual prophylactic stations, where the purchase by the hypochondriac of that universal panacea, Alka-Seltzer, is supposed to prevent the worst. If to this group of distracted citizens one adds the large number of food faddists who, by similar urges, are persuaded to ingest ever-increasing amounts of pineapple, orange and tomato juice, in order that they, too, may dwell in safety on the alkaline side, it sometimes seems surprising that a normally acid urine is now ever encountered!

The sad part of this erroneously held belief is that there is no evidence to show that an acid urine is irritating, or that an alkaline urine is soothing. The pertinent point is that irritation, frequency and other symptoms associated with urinary infection are the result of the infecting organisms and their by-products, not the result of the reaction of the urine.

METHENAMIN

In our attempt to rid our patient of these various organisms, let us first consider the efficiency of our oldest urinary germicide—methenamin. It is cheap, it has been used for years, and is known to be free of dangers; I have never heard of a death resulting from its administration. To be effective, the urine must be acid in order to liberate formaldehyd, and it is evident that this must be present in the urine in sufficient strength and of long enough duration to be germicidal. If the concentration of methenamin in the urine is .5 per cent and its p^H is 6, bacteria will survive for twenty-four hours; but if the p^H is lowered to 5, it will become sterile in six hours. So it is obvious that it is as important to increase the acidity of the urine as to increase the dosage of the drug to obtain the maximum of germicidal effect. In fact, so many patients are sensitive to formaldehyd that the administration of too large doses of methenamin may lead to a bladder irritability quite as annoying as that caused by the infection itself, and hematuria has not infrequently been produced by the drug alone.

Except for this drawback, methenamin is an ideal urinary antiseptic, inexpensive and efficient. In cases where there tends to be any retention of urine from atony of the bladder musculature, the administration of methenamin may cause sufficient vesical irritation to result in better emptying.

KETOGENIC DIET AND URINE

In 1931 Helmholz noticed that the urine of his epileptic patients who were on a ketogenic diet did not become foul after standing. He reasoned that this urine must contain some bacteriostatic or bactericidal property not present in normal urine. He, naturally, investigated the possibility that its diacetic content was responsible, but as many colonies grow in urine with .5 per cent diacetic as that without, while in ketonurine growth it was much diminished.

At almost the same time that Helmholz was investigating the cause of the bactericidal effects of

ketonurine, Anson Clark was searching for some drug or diet that would inhibit the growth of colon organisms. Being informed by Barborka of the extreme degree of acidity produced by the ketogenic diet in children with epilepsy, he at once applied the diet to a large series of adults having urinary infections with surprising clinical results.

Helmholz, having demonstrated that the germicidal properties of this urine were due neither to its acidity nor its diacetic acid content, it was not long before A. T. Fuller of England discovered that the germicidal factor was Levor rotary beta-oxybutyric acid. He published his findings in 1933, and it was soon conclusively shown that this acid in concentrations of 0.5 per cent or below was not only bacteriostatic, but definitely bactericidal. But the efficiency of its germicidal effect remained in direct proportion to the p^H of the urine.

Since beta-oxybutyric acid is difficult to manufacture, and is also unstable when taken by mouth except for individuals already in ketosis, M. L. Rosenheim searched through the organic acids for one that would be excreted unchanged in the urine. With such an acid he hoped to duplicate the effect of beta-oxybutyric. Schotten in 1883, and Knoop in 1905, had showed mandelic acid to be excreted unaltered in the urine. Being used extensively in photography, it was readily available, and Helmholz injected 700 centimeters of a one per cent solution into a dog over a seven-hour period, during which time the concentration of mandelic acid in the urine varied from 1.5 to .5 per cent. The blood urea and urea clearance tests both showed a temporary insult to the kidney as a result of this injection, with complete recovery some three days later.

When given to a patient in doses of three grams of a 10 per cent solution four times a day, the concentration of the drug in the urine rises rapidly to over one per cent; and at a p^H of five a concentration of .25 per cent proves bactericidal for most organisms. As in the case of beta-oxybutyric acid, the lower the p^H of the urine the lower is the concentration of mandelic acid necessary to secure bactericidal action. In a series of experiments the bactericidal action of normal urine, to which one per cent of mandelic acid had been added, was found to correspond closely to that of urine to which the same concentration of acid was present on excretion.

Experience has demonstrated that mandelic acid is most satisfactorily administered in the form of its sodium salt neutralized by sodium bicarbonate, and dispensed as a liquid flavored with lemon syrup. A gram of ammonium chlorid should be dispensed with each dose to insure the most effective germicidal p^H level.

In the presence of urea-splitting organisms, such as the proteus ammonia and pseudomonas, the lowering of the p^H may prove difficult or sometimes even impossible to accomplish. In such cases ammonium nitrate, dilute hydrochloric or even nitrohydrochloric, should be tried in association with an acid-ash diet. Such patients should be impressed with the contraindication to the ingestion of citrus

fruits, milk of magnesia, or the consumption of large quantities of spinach, celery and other foods of high alkaline-ash content.

If renal function is poor, there is the possibility of producing an acidosis, and it may be impossible with such impairment to obtain sufficient concentration of mandelic acid in the urine to be effective. Under such circumstances the most recent of our urinary antiseptics should be employed.

SULFANILAMIDE

The history of sulfanilamide demonstrates how tedious are our advances in therapy, and illustrates how indebted is the medical profession to the labors of those in other fields of science. Physicians are inclined to forget that neither Pasteur, Roentgen nor Currie held M. D. degrees, and few urologists feel any debt of gratitude or, in fact, remember that Arthur Binz, a German chemist, made intravenous urology possible by his synthesizing uroselectan. So with sulfanilamid the profession is again in deep debt to the chemists of the dye industry that developed this drug.

As soon as the bactericidal properties of sulfanilamid were demonstrated, the determination of dosage and discovery of its toxic effects rapidly followed, and quite as rapidly confusion in its nomenclature developed as different chemical houses applied proprietary names, such as prontylin, prontosil, allum, streptocide, et cetera; so that the Council on Pharmacy and Chemistry of the American Medical Association has adopted the term "sulfanilamid" as a nonproprietary name, and has declared that it is unfortunate that the term "prontosil" is used in this country for a compound not identical with the product that has been used in Europe.

Employed first as a specific agent against streptococcal infections, it has proved equally effective in the urinary tract against the Escherichian coli, while paradoxically it has no effect against streptococcus fecalis. It was soon discovered that larger doses of the drug are better tolerated by the patient in bed, and that much smaller doses must be used in the ambulatory cases. Apparently, a concentration of ten milligram per cent in the blood serum is sufficiently large to insure a germicidal effect in the urine, and this can be obtained by administering 40 to 60 grains a day in ambulatory cases. Reactions vary and must be warned against; happily, if the drug is discontinued at once they subside rather rapidly. The most annoying, although not most serious, are the skin reactions most likely to occur in warm weather, and characterized by extensive erythema and moderate vasculature. When large doses are given, the blood counts require careful checking, as the destruction of red blood cells has been known to be as high as a million in twenty-four hours.

If the urine is not rendered sterile in a two weeks' period, one may be certain that some abnormal anatomical condition is preventing proper drainage, or that one of the organisms—such as streptococcus fecalis or areabacteric areagenis—is present, and that the battle is going to be hard and long-fought.

It apparently has little effect on streptococcus fecalis, which is the specific organism of impetigo and frequently seems as difficult to eradicate from the urinary tract as from the skin. This organism probably never occurs as a natural invader of the urinary tract, but is carried in on instruments or catheters improperly sterilized. In stained smears it is characterized by the organisms occurring as oval cocci joined together by a refractive streak down the center. When a urinary infection has not responded to this type of therapy, the presence of this organism should be suspected. The administration of the drug by mouth appears to give better results than its administration by needle, and the new form of the drug dispensed under the name of "Neoprontosil," while unquestionably less toxic, seems also less efficacious.

Another advantage of this drug over other urinary germicides is its effectiveness in an alkaline media. So many urinary infections are mixed in character, and not infrequently one of the organisms will be capable of splitting urea into ammonia, so that the possibility of receiving any therapeutic effect from either mandelic acid or methenamin is nil. The pseudomonas and proteus group of organisms are the chief offenders in this respect, although there are some of the cocci that seem but slightly less efficient in the production of ammoniacal urine.

One of the most frequent causes of failure in the treatment of urinary-tract infections in the male is the reinfection of the urine from chronic foci in the prostate. Sulfanilamid is found in the prostatic secretion and would appear, therefore, to be particularly indicated in these cases. Were it not for its distressing side reactions, this drug would indeed seem the ideal urinary antiseptic, but its untoward reactions seem the thorn of this particular rose.

Coccus infections of hematogenous origin, as described earlier in this paper, seem to be little affected by either mandelic or prontosil therapy, while those of the ascending type usually respond to one or the other. Fortunately, the hematogenous type of infection is, in the majority of cases a self-limited affair, from which the patient recovers; but when it assumes a chronic form, treatment by neoarsphenamin has proved the most successful drug for its eradication. Its mode of action is still in dispute, but Pace believes sufficient arsenic is eliminated in the urine to produce a bactericidal effect. This seems somewhat doubtful, however, as such infections, when limited to the bladder, do not respond as well as do those in which the kidneys are also involved. The most efficient and best tolerated dosage scheme is to give two-tenths grams, followed in five or six days by three-tenths grams. If no improvement is noted after these two injections, it is rare for a third dose to produce good results. The elimination of foci in the cervix, prostate, teeth, and tonsils in this type of infection is most important, and until taken care of recurrences seem certain.

IN CONCLUSION

In conclusion, it seems well to emphasize that in the treatment of urinary-tract infections we now have available four efficient drugs, namely,

methenamin, mandelic acid, sulfanilamid, and neoarsphenamin. If cases of such infection do not respond to their proper therapeutic administration, the probabilities are great that there are associated pathological conditions in the form of stone, obstruction, stasis or neoplastic disease, which demand thorough investigation by your urological colleague.

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DISCUSSION

CHARLES PIERRE MATHÉ, M.D. (450 Sutter Street, San Francisco).—Doctor Bumpus' timely paper, dealing with the rapidly changing treatment of infection of the genito-urinary tract, will aid in clarifying this obscure subject in the minds of general practitioners. Unfortunately, in our enthusiasm to employ new medicaments, represented as the last word in urinary antiseptics, one is liable to overlook certain fundamental principles of treatment that have stood the test of time and that are so necessary for eradication of infection of the genito-urinary tract. The essayist does well to emphasize the fact that the infecting organism should be identified before it is attacked by a bactericide. Good, well-stained smears of urinary sediments are not so difficult to make if one will only take the necessary time and trouble, and then one can always intelligently supplement his studies by culture and animal inoculation. In patients in whom infection persists in spite of the administration of antiseptics that the physician has chosen to administer, further urologic investigation should be carried out. In these patients, stasis is the most common cause of persistent infection. We have seen a number of cases presenting resistant chronic infection in the kidney which cleared up permanently after relieving obstruction, viz., dilatation of a ureteral stricture, corrective plastic repair of hydronephrosis, and suspension of an obstructed, ptosed kidney. Other causes for persistent urinary infection are stone, vesical neck obstructions, foreign bodies, neoplasms, etc. It is obvious that, although infection can be ameliorated in these patients by the use of urinary antiseptics, definite relief cannot be obtained without eradication of the predisposing cause.

Out of the large number of available antiseptics, Doctor Bumpus has chosen four that he feels are most efficacious in combating the different types of urinary infection. These are: methenamin, mandelic acid, sulfanilamid, and neoarsphenamin. To this list I would add methylene blue, whose germicidal effect against cocci, particularly the staphylococcus, has been definitely proved. It is less powerful than sulfanilamid, but is indicated when this drug is poorly tolerated. Methylene blue may also be used to supplement sulfanilamid, in which case it aids in the elimination of that drug, counteracts toxicity, decreases the severity of methemoglobinemia occurring in sensitive patients as well as prolonging bactericidal action. I do not feel that pyridium, propokol, salol and other antiseptics should be condemned. They have their place, affording relief to certain patients who fail to respond to the four drugs enumerated above; and they are also efficacious in others in whom they are not tolerated.

I am heartily in accord with the opinion that methenamin is an efficient urinary antiseptic, provided that the urine has been properly acidified. We have found its intravenous use, injecting two grams of this drug daily, most efficacious for the treatment of urinary fever, the well-known syndrome of chills and fever that sometimes follows instrumentation. We feel that in many of these cases fever is due to invasion of the blood stream by infecting organisms. Strange as it may seem, we have been able to prevent the development of this type of bacteremia by the previous empirical administration of quinin.

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HARRY W. MARTIN, M.D. (6253 Hollywood Boulevard, Los Angeles).—Doctor Bumpus has given us a very timely paper and one that should be studied by every general practitioner, because urinary antiseptics at this time are a matter of great discussion between physicians and surgeons, and also the laity as well.

It must be borne in mind that, with any infection in the urinary tract, drainage is the most important factor in its treatment, and no urinary antiseptic can be efficient if obstruction to drainage is present.

Another notable point that Doctor Bumpus has brought out is the significance of the Gram stain, which is sufficient for the diagnosis of urinary sediment and more accurate than cultures. Many physicians are of the opinion that in order to diagnose the majority of urinary-tract infections it is necessary, as Doctor Bumpus points out, to have cultures made. The Gram stain is the most efficient aid we have and everyone can avail themselves of it, and only in certain cases is it necessary for extra laboratory work.

Another point of Doctor Bumpus' worth noting is the necessity of catheterization following operative procedure. Years ago it was taught that catheterization should be resorted to only after every other procedure to empty the bladder had failed, with the result that more damage was done by the distended bladder and its back-pressure changes on the kidneys than could ever be done by catheterizing.

Methenamin is a valuable drug if administered properly when the urine is carefully watched. Fairly large doses should be given if good results are to be obtained, but care must be taken not to cause hematuria.

Sulfanilamide is very likely the most widely discussed drug on the market today, and practically every layman has some slight knowledge regarding it. Like every new discovery, however, care must be taken to see that it is used properly. I recently saw an ambulatory patient who had been taking 80 grains a day for two months, with no change in the urine but a marked change in the blood.

I am firmly of the opinion that if the urine does not show any changes the drugs should be discontinued after two weeks. I also believe that better results are obtained when large doses are given, but that the patient should remain in bed while taking the larger dose.

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FRANK HINMAN, M.D. (384 Post Street, San Francisco).—Between the lines of this report by a specialist, upon the use of urinary antiseptics in general practice, it seems to me that I can read doubt and uncertainty. In his opinion, only four of the myriads of drugs advertised and advocated are at all reliable, and he shows that the potency of each one of these is largely contingent. My own incredulity as to the efficacy of casual medication in the treatment of infections of the urinary tract, as well as my firm conviction that therapy should never replace diagnosis in these conditions, and that when so used it only hinders diagnosis, lets me imagine the more easily, perhaps, this meaning in Doctor Bumpus' paper. His pessimism is fully shared. Most urologists seldom use other drugs than hexamethylenamin, one form or another of mandelic acid—of which a calcium salt has seemed to some less disturbing to most digestive tracts than the sodium—sulfanilamide and arsphenamin. It is important, of course, to know the limitations of use and the prerequisites for greatest efficiency, so ably outlined by Bumpus, of each of these internal urinary antiseptics. Each drug has its own particular field of usefulness, and each, as a rule, acts best only under certain particular circumstances; how useless, for example, are the first two, without proper urinary acidity! Ahead of knowing these contingencies, however, I should place knowledge of the urinary infections themselves. In my opinion, greater attainments are to know well all of the clinical possibilities in both the upper (renal) and lower (urogenital) tracts when pus and organisms occur in the urine; to know when to suspect urinary sepsis as the cause of fever and prostration even in the presence of a negative urine; and, above all, with the clinical induction of the full significance of his history as a guide, to know how to examine the patient for the purpose of diagnosis. The services of a specialist are not required for preliminary studies of this kind, and the routine use of internal urinary antiseptics without such studies is malpractice. The mind of an experienced clinician follows a very simple but logical deduction as facts and findings are brought to it step by step with the history, physical examination and course of clinical events.

The history gives the first lead (the sex, the age, the complaint, and the clinical coincidences). The physical examination gives the next cue (pulse, temperature, palpation

of the kidney area, external genitalia, etc.), and then, in the order indicated, laboratory and special investigations (blood counts, urine examinations, particularly the "three glass test," or two if preferred, rectal [and vaginal] examinations with a study of the prostatic secretion, exploration by x-rays, functional tests, occasionally intravenous urograms) will enable the trained clinician to make a very close, if not correct, deduction of the condition, enough at least to tell him whether or not to put his trust wholly in internal urinary antiseptics. *The dangers of procrastination grow greater and greater as urinary antiseptics grow better and better.* Why all this excitement when the ingestion of a few pills clears the urine? The wise doctor, knowing that most urinary infections are secondary, will suspect other trouble even when successful with his pills. He will not be satisfied until all the findings, gradually collected step by step by means of the preceding studies, either demonstrate the suspected pathologic changes or prove that his suspicions were false. In the course of such investigations he may conclude that the services of a specialist are in order (residual urine, cystoscopy? ureteral catheterizations?). Nevertheless, by his knowledge of infections of the urinary tract and his ability to carry out, not as a routine but as indicated, these simple preliminary steps of investigation for which the services of a specialist are not needed, is established the degree of his clinical wisdom. Few conditions exact a graver price for rough handling and mismanagement. None of the preceding studies, however, is instrumental, and all, when rightly used, are perfectly safe. Answers to queries raised by each step of examination are necessary if the clinician expects to meet, in the best scientific manner, the many contingencies of efficiency in the use of internal urinary antiseptics. By the nature of these answers, their fullness and accuracy, is measured his prescience as a clinician. Clinical sagacity in choosing the right road to a correct diagnosis of infections of the urinary tract is the incidental essence of success in their treatment with internal urinary antiseptics.

THE LURE OF MEDICAL HISTORY†

MEDICINE IN COLONIAL AMERICA*

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I

IN a time when medical knowledge has progressed far beyond the scope and imagination of its primitive days, it is natural that we should have forgotten the story of Colonial America's medicine. The worthy preacher has won admiration for his labors, and the legal man's services have rightly received the praise of later generations, but the doctor, crude though he may have been, has been allowed to sink into an unwarranted oblivion. Church and court have not been radically altered; we feel in them strong ties to the past. Medicine, on the other hand, has gone far from the men and practices of the sixteenth and seventeenth centuries. The pioneer ministry of healing, consequently, seems but the most bizarre of unrelated fancies.

† A Twenty-Five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of CALIFORNIA AND WESTERN MEDICINE. The column is one of the regular features of the Miscellany department, and its page number will be found on the front cover.

* From the Department of History, Stanford University. The author prepared this essay a number of years ago when he was an undergraduate. The friendly interest of an esteemed colleague in the Stanford Medical School has induced him to overcome his hesitations and offer the study to a wider circle of readers.